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NAFITHROMYCIN: A GENERATION MACROLIDE ANTIBIOTIC WITH ENHANCED EFFICACY AGAINST GRAM POSITIVE BACTERIA

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ABSTRACT

The first new antibiotic in its class developed world wide over 3- decades. It is 10 times more effective than azithromycin it achieves comparable results with 3-days treatment. Regimen nafithromycin is a Novel third-generation macrolide antibiotic belonging to the ketolide subclass. It is derived from the erythromycin and exhibits enhanced activity against a broad spectrum of bacterial pathogens, including macrolide resistant strains of streptococcus pneumonia & staphylococcus aureus Nafithromycin remains an important option in the management of bacterial infections preclinical and clinical studies have demonstrated nafithromycin efficacy in treating respiratory tract infections. Nafithromycin way granted "qualified infectious disease product" (QIDP) status by the US Food & Drug Administration (USFDA). Nafithromycin is powerful and effective against Community & Acquired bacterial pneumonia (CABP) a Serious from of pneumonia Caused by drug resistance bacteria After 3- decades of research and hard work, India to has to led the way with the Creation to "Nafithromycin the Country's first indigenous macrolide antibiotics".

Keywords: Antimicrobial resistance (AMR) Community-acquired bacterial infections, anti-bacterial activity, pneumonia treatment, broad spectrum activity, Gram positive bacteria.

INTRODUCTION

Nafithromycin is a relatively layer - known antibiotic that belongs to the macrolide class of drugs. it's primary used for it's bactericidal and bacteriostatic properties making of effective in treating a variety of bacterial infections preclinical studies have shown that "Nafithromycin has pharmacodynamic action against macrolide and ketolide resistant strains of streptococcus pneumonia. Nafithromycin works by inhibiting bacterial protein synthesis through binding to the 50s ribosomal subunit, effectively blocking peptide elongation it's pharmaco kinetic Profile include good oral bioavailability and tissue penetration, particularly in respiratory tissue making it effective for treating infections like pneumonia and bronchitis. "Dr. Jitendra singh" described the three-day treatment regimen of Nafithromycin as a game change r in addressing drug resistant pneumonia, a condition responsible for over two million deaths globally each year Nafithromycin was developed to address certain bacterial strains that have become resistance to older antibiotics It Offers an alternative to other macrolides like Azithromycin & clarithromycin, Nafithromycin primary therapeutic applications involved the treatment of a variety of bacterial infections. Nafithromycin is specially formulated to treat Community - Acquired Bacterial Pneumonia (CABP) severe for illnesses caused by antibiotic resistance bacteria it effectively targets both typical and atypical pathogens. The drug is particularly beneficial from vulnerable populations including children, the elderly & individually with weakened immune system Nafithromycin has the potential to save countless liver by preventing complications from CABP. Nafithromycin is a macrolide

antibiotic known for its broad-spectrum activity against various bacterial pathogens.

It has gained attention due to its efficacy in treating respiratory infections, skin and soft tissue infections, and other bacterial diseases. This review article provides an overview of Nafithromycin's mechanism of action, pharmacokinetic properties. The first generation of this class includes naturally occurring 14 membered ring macrolides such as erythromycin, exhibiting the extent of inducer ability along with potent activity against *Streptococcus aureus*. Macrolides from second generation includes 14 or 16 membered semisynthetic compounds, which gives rise to a mutation into constitutive MLS resistance to macrolide antibiotics. Third generation macrolides increase the acid stability of the 14 membered ring macrolides and includes a 15 membered ring macrolide azithromycin, thereby their pharmacokinetics are improved which also reflected in the broadening in antibacterial spectrum of this generation.

THE JOURNEY OF DEVELOPMENT

Dr. Jitendra Singh announces soft launch of India's first indigenous antibiotic nafithromycin to combat drug Resistance. Minister of Science and Technology, launched the drug in New Delhi.

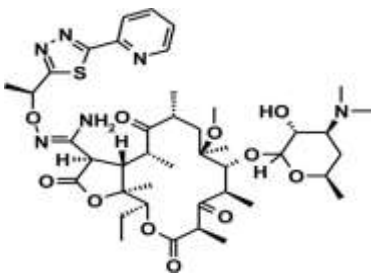
RESEARCH AND DEVELOPMENT

Years of research:

- Nafithromycin is the result of 14 years of research and an investment of rs500 crore (around $60 million).
- The drug went through clinical trials in the and India before being approved.

Support and Manufacturing:

- Nafithromycin was developed with the help of the Biotechnology Industry Research Assistance Council (BIRAC), a government agency in India.
- It will be sold under the brand name Miqnaf by Wockhardt Pharmaceuticals, making it available to more patients.



Nafithromycin structure

DRUG PROFILE

Generic name: - Nafithromycin.

Background: - Nafithromycin is under investigation in clinical trial NCT02903836 (Phase II Study of oral Nafithromycin in CABP).

Type: - Small molecule.

Chemical Formula:- $C_{42}H_{62}N_6O_{11}S$

Nafithromycin's Role in Addressing Antimicrobial Resistance (AMR)

Antimicrobial resistance (AMR) is one of the most critical global health challenges today. The overuse and misuse of antibiotics have led to the development of resistant bacterial strains, which makes infections harder to treat and results in prolonged hospital stays and higher healthcare costs. Nafithromycin has been developed, in part, to combat this growing concern. The drug is more resistant No bacterial efflux pumps and enzymatic degradation mechanisms that often render older antibiotics ineffective. This helps in addressing infections caused by **multi-drug-resistance (MDR)** bacteria, which are a growing concern in both **developed** and **developing nations**.

1. Alternative to First-Line Antibiotics

Nafithromycin can be used as an alternative to more commonly used antibiotics such as **Azithromycin** and **Clarithromycin**, especially in cases where bacterial resistance to these drugs is prevalent.

2. Targeting Resistant Strains

Nafithromycin is effective against a variety of resistant strains of **Streptococcus pneumoniae** and **Staphylococcus aureus**, both of which have become resistant to many conventional antibiotics over time.

More Powerful and Effective

1. Nafithromycin is 10 times stronger than Azithromycin, meaning it works much better at fighting resistant bacteria.
2. It reaches the lungs 8 times better than Azithromycin, which is important since pneumonia mainly affects the lungs.

Spectrum of Activity

Nafithromycin is effective against a variety of both gram-positive and gram-negative bacteria. It is particularly used for treating respiratory tract infections, skin infections, and gastrointestinal infections. Nafithromycin is also effective against certain atypical pathogens like Mycoplasma pneumoniae and Chlamydia pneumoniae, which are known to cause respiratory diseases.

Some of the bacteria Nafithromycin targets include

- ✓ Streptococcus pneumoniae (causing pneumonia)
- ✓ Haemophilus influenzae (associated with upper respiratory tract infections)
- ✓ Mycoplasma pneumoniae
- ✓ Chlamydia pneumoniae
- ✓ Staphylococcus aureus

Nafithromycin is Important for India

Cost-Effective Treatment: Nafithromycin could lower healthcare costs by improving patient recovery and reducing the need for long hospital stays.
It also prevents the use of treatments that don't work, which can be expensive.

Fighting AMR: As a new antibiotic, Nafithromycin can help fight the problem of antimicrobial resistance (AMR), a glowing global health threat.

Developing new antibiotics is crucial in stopping the spread of infections that cannot be treated with current drugs.

Global Health Emergency: AMR has reached crisis levels globally, and the development of new antibiotics has stalled since the 1980s. Nafithromycin is the first new antibiotic developed in India in the last 30 years.

Need for New Antibiotics: Existing antibiotics have become ineffective against superbugs. Nafithromycin can treat infections caused by bacteria that are resistant to current antibiotics.

Safety and Tolerability: The drug has shown minimal side effects and is well-tolerated by patients, making it a safer option for a wider population, including those with comorbid conditions.

Mechanism of action: Nafithromycin is a newer antibiotic in the ketolide class. Here's a simplified flowchart of its mechanism of action:

Step 1: Drug Entry
Nafithromycin enters bacterial cells via passive diffusion or specific transport mechanisms.

⬇

Step 2: Target Binding
The bacterial Binds to the 50S ribosomal subunit of ribosome.

⬇

Step 3: Inhibition of Protein Synthesis
Prevents proper functioning of the ribosome by blocking the translocation step, where the growing peptide chain moves from the A-site to the P-site during translation.

⬇

Step 4: Disruption of Bacterial Function
Inhibits bacterial protein synthesis, affecting vital proteins required for growth and replication.

⬇

Step 5: Bacteriostatic or Bactericidal Effect
This inhibition leads to a bacteriostatic effect (stopping growth) or a bactericidal effect (Killing bacteria), depending on the organism and drug concentration.

Pharmacological action of Nafithromycin:
Target: Nafithromycin binds to the bacterial 50s ribosomal submit.

Effect: It inhibits bacterial protein synthesis by interfering with the Elongation of the peptide chain during translation.

Unique Action: unlike traditional macrolides, Nafithromycin exhibits a dual binding mechanism. To the ribosome, enhancing its efficacy and reducing bacterial resistance.

Pharmacokinetics:
Absorption: - Nafithromycin is generally well absorbed when taken orally.

Distribution: - It's is widely distributed throughout the body including the lungs making it effective in treating respiratory tract infections.

Metabolism: - Nafithromycin is metabolized in the liver through it's exact metabolic pathway may vary depending on individual patient factors.

Elimination: - It's primarily eliminated through biliary excretion. Which means that most of the drug is excreted in the faces, with only a small amount being excreted in the urine.

Dose of Nafithromycin:
For children aged 2 years & older: - The dosing for children typically depends on their age and weight. A typical dose is 5-10mg/kg once a day after for 5-7 days depending on the severity and type of infections.

Maximum dose for children: - The daily dose for children is usually at 400 mg per day for adults & elders.

Adults Standard Dose:-150 mg once daily.

Duration: - The treatment duration is usually 5 to 7 days depending on the type and Severity of the infection.

Elderly Patients: - In elderly patient, the dose is generally the same as for adults, but special care should be taken in Case of renal impairment or other underlying health conditions .The health care provider may adjust the dose based on kidney or liver functions.

Maximum Dose For Adult & Elder:- maximum recommended dose is 400 mg per day.

Food and Drug Interactions:
Food Interactions:
1. Grapefruit & grapefruit juice: Increase the Nafithromycin level and it leads to toxicity.

2. Dairy products: may decrease Nafithromycin absorption.
Drug Interactions:

Warfarin: Nafithromycin may increase warfarin levels and leads to increased risk of bleeding.

Digoxin: Nafithromycin may increase digoxin levels leading to toxicity.

Statins: Nafithromycin may increase statin levels leading to increased risk of myopathy.

Contraindications of Nafithromycin: Hypersensitivity, Sever Liver Disease, Sever Kidney Disease, Pregnancy and Lactation.

Side Effects
Like other antibiotics, Nafithromycin can cause side effects, although they are typically mild and transient. Common side effects include

Gastrointestinal disturbances such as nausea, vomiting, or diarrhoea.

Allergic reactions like rash or itching.

Liver enzyme elevation, although this is less common and usually reversible after discontinuing the drug.

QT interval prolongation: This is a potential concern for patients with a history of cardiac conditions or those on certain medications that affect heart rhythm.

Therapeutic Uses of Nafithromycin
Nafithromycin's primary therapeutic applications involve the treatment of a variety of bacterial infections. Its uses include:

1. Respiratory Infections
Nafithromycin is commonly prescribed for upper and lower respiratory infections caused by susceptible bacteria. This includes **community-acquired pneumonia**, **sinusitis**, and **bronchitis**. Given its broad-spectrum activity, it is particularly effective in treating infections caused by **atypical pathogens** such as **Mycoplasma pneumoniae** and **Chlamydia pneumoniae**.

2. Skin and Soft Tissue Infections
The drug is also used for the treatment of skin and soft tissue infections caused by bacteria like **Staphylococcus aureus** and **Streptococcus pyogenes**. This includes conditions like cellulitis, impetigo, and abscesses.

3. Urinary Tract Infections
Nafithromycin may be used for certain urinary tract infections, particularly those caused by susceptible organisms like **E. coli**.

4. Gastrointestinal Infections
Some gastrointestinal infections caused by atypical bacteria, such as **Helicobacter pylori**, can be treated with Nafithromycin, though this is less common than other first-line therapies.

5. Prevention of Bacterial Endocarditis
Although not a first-line agent, Nafithromycin may be used in specific cases as a prophylactic measure against **bacterial endocarditis**, particularly in patients with a high risk of infection due to heart valve issues.

CONCLUSION

Nafithromycin is a promising macrolide antibiotic that has shown effective antimicrobial activity, particularly against a range of Gram-positive pathogens and certain Gram-negative organisms. Its mechanism of action, which involves inhibition of bacterial protein synthesis, is consistent with other drugs in its class, though it also demonstrates a favourable pharmacokinetic profile, including longer half-life and less frequent dosing. Nafithromycin's side-effect profile is generally favourable, with fewer gastrointestinal disturbances and a reduced risk of QT prolongation compared to some other macrolides. However, resistance patterns and its place in therapy relative to other antibiotics require further investigation. In the future, clinical studies focusing on Nafithromycin's role in treating specific infections, its effectiveness in combination therapies, and resistance management will be essential for establishing its optimal use in clinical practice.

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